The present invention relates to an immunoassay for detecting an antigen in a sample. An important feature of the present method is that two antibodies are used to bind the antigen, and each antibody is contacted with the sample sequentially to form an agglutinate comprising the antigen and the two antibodies (see (i) and (ii) in Claims 7 and 21). Therefore, formation of the agglutinate in the claimed method is accomplished by a two-step antibody binding reaction. Another important feature of the claimed method is that the amount of agglutinate is measured optically (see (b) in Claims 7 and 21). The present inventors have discovered that this two-step antibody binding reaction provides a assay method having high sensitivity and low cost.

The rejection of the claims under 35 U.S.C. §102(b) or, in the alternative, under 35 U.S.C. §103(a) over Cragle et al (WO 85/02258) is respectfully traversed. This reference fails to disclose or suggest the claimed immunoassay method.

Cragle et al disclose an immunoassay for assaying for the presence of an antigenic substance (Ag) in a fluid (i.e., sample) (see the Abstract). In each of the embodiments disclosed by this reference, at least one of the antibodies is labeled (see pages 5-6). In order to determine the amount of antigen present in the solution, the presence of the label is used as an indicator (see the Examples at pages 10-17 of the reference). Cragle et al fail to disclose formation of an agglutinate comprising the antigen and the antibodies, and detecting the amount of agglutinate in the solution. The reference fails to disclose the claimed invention.

Moreover, Cragle et al fail to suggest the claimed method. One of the antibodies in the method disclosed by the reference is labeled. This label is used to measure the amount of antibody-antigen complex formed in the assay. The reference fails to even disclose that an

agglutinate is formed in the sample, let alone measuring the amount of the agglutinate formed as recited in the claimed immunoassay. Cragle et al fail to suggest the claimed immunoassay.

Cragle et al fail to disclose the immunoassay recited in Claims 7 and 21. Claims 7-34 are not anticipated by or obvious over this reference. Withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §102(b) or, in the alternative, under 35 U.S.C. §103(a) over Abstract 94-295892/199437 is respectfully traversed. The Abstract corresponds to EP 0 617 285 (EP '285; IDS reference AL), which is a German language document. Applicants enclose herewith an English translation of EP '285. All citations to EP '285 refer to the English translation.

EP '285 discloses a method for determining an analyte, i.e., an antigen, in a sample by contacting the analyte with a single solution that contains a receptor R_1, e.g., an antibody, immobilized on a particulate carrier that is capable of binding specifically with the analyte and a soluble receptor R_2, e.g., a second antibody, that is also capable of binding the analyte (see the Abstract; page 3, lines 5-8; and Example 1 at page 7 under Test Procedure). In the assay disclosed in this reference the antibody binding reaction is conducted in a single step. The sample is not sequentially contacted with R_1 and then R_2. The sample containing the analyte is contacted with a single solution containing both R_1 and R_2 to form an complex between the analyte, R_1, and R_2.

In contrast, the claimed immunoassay specifies *sequentially* contacting the sample with the first antibody *and then* with the second antibody, to form the agglutinate. EP '285 fails to disclose the claimed immunoassay. In the assay disclosed by the reference, the sample is contacted with R_1 and R_2 at the same time. The sample is not sequentially

contacted with R1 and then R2. EP '285 fails to anticipate the claimed immunoassay.

Moreover, the reference fails to even suggest the claimed method. The purpose of the method disclosed in EP '285 is limiting or preventing the hook effect in the assay (see page 4, lines 3-4). This purpose is accomplished by using a solution containing R_1 and R_2, and contacting this solution with the sample containing the analyte (see page 4, lines 5-8). Therefore, according to EP '285, limiting or preventing the hook effect is accomplished by contacting the analyte with R_1 and R_2 at the same time. One reading this reference would have absolutely no motivation to contact the analyte with R_1 and then R_2, i.e., contacting the analyte with R_1 and R_2 sequentially, since EP '285 explicitly discloses that the hook effect is reduced or prevented when the analyte is contacted with R_1 and R_2 at the same time, i.e., the antibody solution contains both R_1 and R_2. One with EP '285 would conclude that contacting the analyte sequentially with R_1 and R_2 would not reduce or prevent the hook effect, and have no reason to conduct the assay in this manner. A modification of a method cannot render the method unsatisfactory for its intended purpose (see M.P.E.P. §2143.01, page 2100-110, 111). EP '285 fails to suggest the claimed immunoassay.

EP '285 fails to disclose the immunoassay recited in Claims 7 and 21. Claims 7-34 are not anticipated by or obvious over this reference. Withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112 are believed to be obviated by the amendments submitted above. The claims have been amended for clarity, and to recite the formation of an agglutinate. Withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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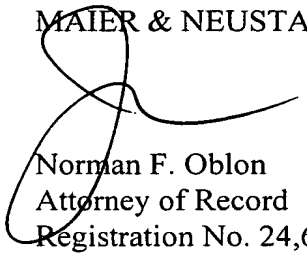

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